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STIC Database Tracking Number: 115454

TO: Kevin Weddington **Location: REM-4C70** **Art Unit: 1614** February 27, **2004** **Case Serial Number: 08/653034**	**From: P. Sheppard** **Location: Remsen Building** **Phone: (571) 272-2529** **sheppard@uspto.gov**

Search Notes

REM-4887

115454

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: K. Weddington H68082

Serial Number: 08/653,034

Date: 2-26-04

Phone: 272-0587

Art Unit: 1614

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

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Date completed: 2/27/04

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Terminal time: _____

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Number of Searches: _____

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_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

_____ Bibliographic

Vendors

_____ IG

_____ STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (8-90)

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FILE COVERS 1907 - 27 Feb 2004 VOL 140 ISS 10
FILE LAST UPDATED: 26 Feb 2004 (20040226/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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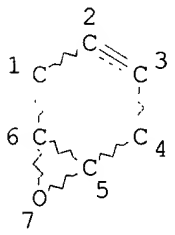
L5 STR



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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE
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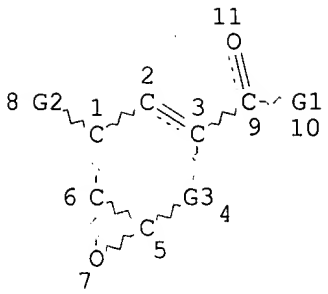
L10 STR



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CH X
@21 22

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VAR G2=OH/20
VAR G3=CH2/21
VAR G4=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/14
REP G5=(3-6) C
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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L12 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

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L12 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319845 HCAPLUS
DOCUMENT NUMBER: 138:337724
TITLE: A method of forming 4-acetamido-3,5-diamino-1-cyclohexene-1-carboxylic acid neuraminidase inhibitors by dynamic combinatorial chemistry, and compounds obtained thereby
INVENTOR(S): Steeneck, Christoph; Eliseev, Alexey V.; Hochguertel, Matthias; Kroth, Heiko
PATENT ASSIGNEE(S): Therascope A.-G., Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033437	A2	20030424	WO 2002-EP11526	20021015
WO 2003033437	A3	20031218		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-328802P P 20011015
US 2002-356731P P 20020215

OTHER SOURCE(S): MARPAT 138:337724

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a group of novel cyclohexenecarboxylic acid-type neuraminidase inhibitors resulting from dynamic combinatorial chem., which was used to evaluate and compare the binding of various amine substitution patterns in this series to the binding site of neuraminidase. In particular, the invention relates to title compds. I [wherein: dotted line = one double bond; R1-R4 = H, C1-C20 alkyl, C2-C20 alkenyl, C4-C20 aryl, C5-C20 aralkyl, C5-C20 alkaryl, all of which can contain N, O, and/or S atoms or be substituted by OH or C1-C4 alkyl ester groups; or one of NR1R2 and NR3R4 is a guanidino group NR5-C(NR6R7):NR8 where R5-R8 = as given for R1-R4; R9 = C1-C4 alkyl group; or a physiol. acceptable salt or solvate in any stereoisomeric form or mixts. thereof in any ratio]. A further object of the invention is a method of forming a library of components which are potentially capable of binding to neuraminidase, in particular influenza neuraminidase, which method comprises: (i) selecting a plurality of mols. carrying a functionality which may interact with a binding site of neuraminidase, said mols. furthermore having a linking group which is capable of interacting with other linking groups under the formation of reversible bonds; (ii) reacting the mols. carrying the functionality with a mol. of I (as above) in the presence of the target, under conditions where a formation of reversible bonds between the linking groups on I and on the mols. carrying a functionality occurs. The method was applied to N-derivatization of II and III [R1 = R2 = H]. Competitive, reversible, and dynamic combinatorial imine formation between I or II [R1 and/or R2 = H] and multiple aldehydes or ketones, in the presence of neuraminidase, followed by irreversible redn. of the imines formed, gave corresponding reductive alkylation products with enhanced inhibitory activity. For instance, combinatorial reaction of scaffold II [R1 = R2 = H] with 10 aldehydes in aq. imidazole buffer in the presence of neuraminidase, and reductive quenching with (Bu4N)BH3CN, gave primarily II [R1 = CH2CH2CH2Ph, R2 = H] and lesser amts. of II [R1 = cyclohex-3-enylmethyl, R2 = H] and II [R1 = PhCH(Me)CH2CH2, R2 = H]. All 3 products had neuraminidase Ki values lower than that of the starting scaffold (31.3 .mu.M), with the major product having the lowest value (1.64 .mu.M). Also explored were scaffolds III, the use of ketones instead of aldehydes, and disubstitution of the 3-amino group. The most preferred resultant compd. is IV, which has neuraminidase inhibitory activity comparable to the known, structurally similar, influenza drug oseltamivir.

IT **187226-87-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(scaffold intermediate; prepn. of triaminocyclohexenecarboxylate inhibitors of neuraminidase by dynamic combinatorial chem.)

IT **76985-84-7**

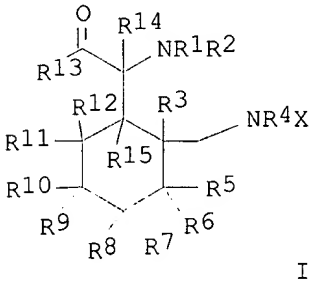
RL: RCT (Reactant); RACT (Reactant or reagent)
(scaffold precursor; prepn. of triaminocyclohexenecarboxylate inhibitors of neuraminidase by dynamic combinatorial chem.)

L12 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:690155 HCAPLUS
DOCUMENT NUMBER: 137:232486
TITLE: Synthesis of combinatorial libraries of compounds reminiscent of natural products
INVENTOR(S): Schreiber, Stuart L.; Shair, Matthew D.; Tan, Derek S.; Foley, Michael A.; Stockwell, Brent R.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: U.S., 129 pp., Cont.-in-part of U.S. Ser. No. 951,930.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6448443	B1	20020910	US 1998-121922	19980725
WO 2000006525	A2	20000210	WO 1999-US16753	19990722
WO 2000006525	A3	20001116		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9953200	A1	20000221	AU 1999-53200	19990722
US 2003082830	A1	20030501	US 2002-185364	20020627

PRIORITY APPLN. INFO.:
US 1996-29128P P 19961016
US 1997-49864P P 19970606
US 1997-951930 A2 19971015
US 1998-121922 A 19980725
WO 1999-US16753 W 19990722

OTHER SOURCE(S): CASREACT 137:232486; MARPAT 137:232486
GI



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AB The present invention provides complex compds., e.g., I [R1, R2, R4 - R8, R10- R12, R14 - R18, X = H, linear or branched (un)substituted alkyl, aryl, alkenyl, aminoalkyl, acylamino, acyloxy, alkoxycarbonyl, alkoxy, alkylaryl, hydroxyalkyl, thioalkyl, acyl, NH2, OH, SH, aryloxy, alkylthio, arylalkoxy, alkynyl, halogen, CN, CONH2, NO2, CF3, phosphine, heterocycle; R2R3 = O, NO; R3 = OR16; R8R9 = epoxide; R9 = OR17; R12R13 = O (.gamma.-lactone); R13 = OR18, NHR18], reminiscent of natural products and libraries thereof, as well as methods for their prodn. The inventive compds. and libraries of compds. are reminiscent of natural products in that they contain one or more stereocenters, and a high d. and diversity of functionality. In general, the inventive libraries are synthesized from diversifiable scaffold structures, which are synthesized from readily

available or easily synthesizable template structures. In certain embodiments, the inventive compds. and libraries are generated from diversifiable scaffolds synthesized from a shikimic acid based epoxyol template. In other embodiments, the inventive compds. and libraries are generated from diversifiable scaffolds synthesized from the pyridine-based template isonicotinamide. The present invention also provides a novel ortho-nitrobenzyl photolinker and a method for its synthesis. Furthermore, the present invention provides methods and kits for detg. one or more biol. activities of members of the inventive libraries. Addnl., the present invention provides pharmaceutical compns. contg. one or more library members.

IT **206537-16-8P 213027-96-4P**
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of combinatorial libraries of compds. reminiscent of natural products)

IT **106861-59-0 106861-60-3**
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(synthesis of combinatorial libraries of compds. reminiscent of natural products)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:235909 HCAPLUS
DOCUMENT NUMBER: 136:279213
TITLE: Method for preparation of optically active 3-benzhydrylamino-4,5-dihydroxy-1-cyclohexene-1-carboxylic acid esters by optical resolution of racemates
INVENTOR(S): Sugioka, Takashi; Ujita, Katsuji; Kuwayama, Tomoya; Shimizu, Kazuya; Yamanaka, Masayoshi; Ueyama, Shingo; Terajima, Shiro
PATENT ASSIGNEE(S): Kuraray Co., Ltd., Japan; Sagami Chemical Research Center
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002088035	A2	20020327	JP 2000-397595	20001227

PRIORITY APPLN. INFO.: JP 2000-213265 A 20000713
OTHER SOURCE(S): MARPAT 136:279213
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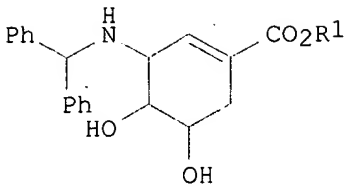

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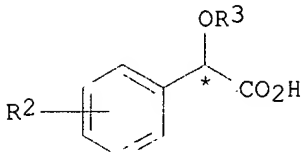

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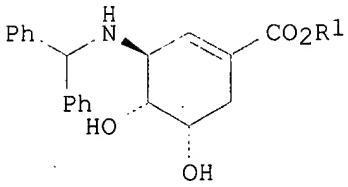

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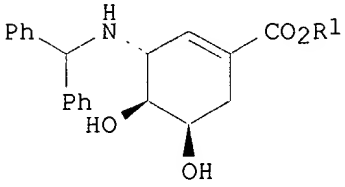


IV

AB Optically active r-3-benzhydrylamino-t-4,t-5-dihydroxy-1-cyclohexene-1-carboxylic acid esters [I; R1 = (un)substituted alkyl, cycloalkyl, aryl, or aralkyl] are prepd. by optical resoln. which involves reaction of optically active mandelic acid derivs. (II; R2 = H, alkyl, alkoxy, halo; R3 = H, alkyl, acyl; * represents an asym. carbon atom) with racemic-I to form diastereomer salts, sepg. one of the optically active diastereomer salts, and reacting the obtained optically active diastereomer salts with base in the presence of water to give (3S,4R,5S)-3-benzhydrylamino-4,5-dihydroxy-1-cyclohexene-1-carboxylic acid esters (III; R1 = same as above) or (3R,4S,5R)-3-benzhydrylamino-4,5-dihydroxy-1-cyclohexene-1-carboxylic acid esters (IV; R1 = same as above). Thus, 3.67 g r-3-benzhydrylamino-t-4,t-5-dihydroxy-1-cyclohexene-1-carboxylic acid Et ester (prepn. given) and 1.52 g (R)-mandelic acid were dissolved in 30 mL anhyd. ethanol under heating, gradually cooled to 20.degree., left to stand at this temp. for 1 h, and filtered to give 2.23 g crystal (43% yield and 64% ee) which was recrystd. four times from anhyd. ethanol to give 0.52 g (R)-mandelic acid (3S,4R,5S)-3-benzhydrylamino-4,5-dihydroxy-1-cyclohexene-1-carboxylic acid Et ester (10% yield and 99.6% ee). The latter diastereomer salt (0.52 g) was stirred with 10 mL 1 N aq. NaHCO3 and extd. with 10 mL EtOAc with stirring at 25.degree. for 30 min to give 0.367 g (3S,4R,5S)-3-benzhydrylamino-4,5-dihydroxy-1-cyclohexene-1-carboxylic acid Et ester (10% yield from the racemate).

IT **182367-90-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of optically active 3-benzhydrylaminodihydroxycyclohexenecarboxylic acid esters by optical resoln. of racemates via diastereomer salt formation with optically active mandelic acid derivs.)

L12 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:434401 HCAPLUS
DOCUMENT NUMBER: 133:177332
TITLE: Studies on the Narciclasine Alkaloids: Total Synthesis of (+)-Narciclasine and (+)-Pancratistatin
AUTHOR(S): Rigby, James H.; Maharoof, Umar S. M.; Mateo, Mary E.
CORPORATE SOURCE: Department of Chemistry, Wayne State University, Detroit, MI, 48202-3489, USA
SOURCE: Journal of the American Chemical Society (2000), 122(28), 6624-6628
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:177332

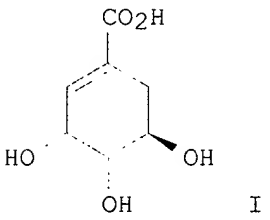
AB Enantioselective total syntheses of the antitumor alkaloids, (+)-narciclasine and (+)-pancratistatin, are reported. These syntheses feature a stereo- and regiocontrolled aryl enamide photocyclization to construct a common, advanced intermediate possessing a trans-fused BC substructure. Differential functional group interchange in the C-ring of this phenanthridone core structure allows for the prodn. of the two target natural products in enantiomerically pure form.

IT **106861-61-4P**
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (+)-narciclasine and (+)-pancratistatin)

IT **106861-60-3P 200182-30-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (+)-narciclasine and (+)-pancratistatin)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:268023 HCAPLUS
DOCUMENT NUMBER: 133:43373
TITLE: An Enantioconvergent Route to (-)-Shikimic Acid via a Palladium-Mediated Elimination Reaction
AUTHOR(S): Yoshida, Naoyuki; Ogasawara, Kunio
CORPORATE SOURCE: Pharmaceutical Institute, Tohoku University, Sendai, 980-8578, Japan
SOURCE: Organic Letters (2000), 2(10), 1461-1463
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:43373
GI



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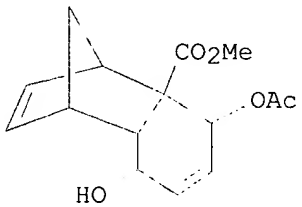

II

AB (-)-Shikimic acid (I), the key intermediate in the shikimate pathway in plants and microorganisms, was synthesized in an enantioconvergent manner from both enantiomeric starting materials by employing a palladium-mediated elimination reaction of II as the key step.

IT **76985-84-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioconvergent route to (-)-shikimic acid via a palladium-mediated elimination reaction)

IT **106861-59-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(enantioconvergent route to (-)-shikimic acid via a palladium-mediated elimination reaction)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:98489 HCAPLUS
DOCUMENT NUMBER: 132:151600
TITLE: Synthesis of combinatorial libraries of compounds reminiscent of natural products
INVENTOR(S): Schreiber, Stuart L.; Shair, Matthew D.; Tan, Derek S.; Foley, Michael A.; Stockwell, Brent R.; Sternson, Scott M.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006525	A2	20000210	WO 1999-US16753	19990722
WO 2000006525	A3	20001116		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6448443	B1	20020910	US 1998-121922	19980725
AU 9953200	A1	20000221	AU 1999-53200	19990722

PRIORITY APPLN. INFO.:
US 1998-121922 A 19980725
US 1996-29128P P 19961016
US 1997-49864P P 19970606
US 1997-951930 A2 19971015
WO 1999-US16753 W 19990722

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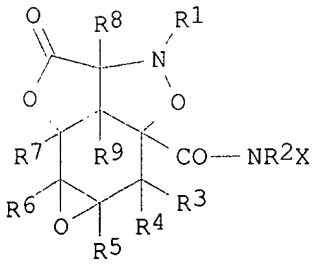


I

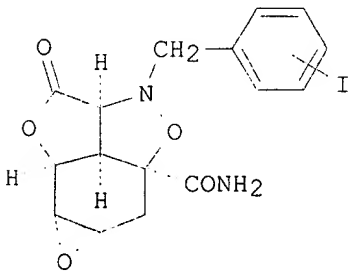
AB The present invention provides complex compds. reminiscent of natural products and libraries thereof, as well as methods for their prodn. The inventive compds. and libraries of compds. are reminiscent of natural products in that they contain one or more stereo centers, and a high d. and diversity of functionality. In general, the inventive libraries are synthesized from diversifiable scaffold structures, which are synthesized from readily available or easily synthesizable template structures. In certain embodiments, the inventive compds. and libraries are generated from diversifiable scaffolds synthesized from a shikimic acid based epoxyol template of formula I [R1-R9 = alkyl, alkenyl, aminoalkyl, acylamino, acyloxy, alkoxycarbonyl, acyl, OH, NH2, aryloxy, halo, CN, nitro, etc.; X = R1, H, solid support unit, biomol., polymer]. In other

embodiments, the inventive compds. and libraries are generated from diversifiable scaffolds synthesized from the pyridine-based template isonicotinamide. The present invention also provides a novel ortho-nitrobenzyl photolinker and a method for its synthesis. Furthermore, the present invention provides methods and kits for detg. one or more biol. activities of members of the inventive libraries. Addnl., the present invention provides pharmaceutical compns. contg. one or more library members.

IT **106861-60-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of combinatorial libraries of compds. reminiscent of natural products)

IT **76985-84-7P 206537-16-8P 213027-96-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of combinatorial libraries of compds. reminiscent of natural products)

L12 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:596166 HCAPLUS
DOCUMENT NUMBER: 132:22896
TITLE: Synthesis and Preliminary Evaluation of a Library of Polycyclic Small Molecules for Use in Chemical Genetic Assays
AUTHOR(S): Tan, Derek S.; Foley, Michael A.; Stockwell, Brent R.; Shair, Matthew D.; Schreiber, Stuart L.
CORPORATE SOURCE: Howard Hughes Medical Institute Department of Chemistry and Chemical Biology and Harvard Institute of Chemistry and Cell Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (1999), 121(39), 9073-9087
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB (-)-Shikimic acid, was converted into both enantiomers of 2-hydroxyoxabicyclo[4.1.0]hept-3-ene-4-carboxylic acid which were attached to a solid support via a photocleavable linker. Tandem acylation-1,3-dipolar cycloaddn. with nitrones yielded tetracyclic templates I. After development of several efficient coupling reactions of I and completion of extensive validation protocols, a split-pool synthesis yielded a binary encoded library calcd. to contain 2.18 million polycyclic compds. These compds. are compatible with miniaturized cell-based forward chem. genetic assays designed to explore biol. pathways and reverse chem.

genetic assays designed to explore protein function. As a simple illustration of the potential of these compds., several were shown to activate a TGF-.beta.-responsive reporter gene in mammalian cells.

IT **106861-60-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of a alkynylbenzyl(acyloxy)benzisoxazoledicarboxamide library for use in genetic assays)

IT **76985-84-7P 106861-59-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of a alkynylbenzyl(acyloxy)benzisoxazoledicarboxamide library for use in genetic assays)

IT **213027-96-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a alkynylbenzyl(acyloxy)benzisoxazoledicarboxamide library for use in genetic assays)

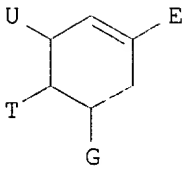
REFERENCE COUNT: 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:582659 HCAPLUS
DOCUMENT NUMBER: 131:228949
TITLE: Preparation of amino acid cyclitols as antiviral agents and neuraminidase inhibitors
INVENTOR(S): Bischofberger, Norbert W.; Kim, Choung U.; Lew, Willard; Liu, Hongtao; Williams, Matthew A.
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: U.S., 157 pp., Cont.-in-part of U.S. Ser. No. 580,567, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5952375	A	19990914	US 1996-606624	19960226
US 5866601	A	19990202	US 1995-476946	19950606
TW 426663	B	20010321	TW 1996-85107487	19960621
US 6225341	B1	20010501	US 1999-288091	19990408
US 2002058823	A1	20020516	US 2000-740504	20001219

PRIORITY APPLN. INFO.:
US 1995-395245 B2 19950227
US 1995-476946 A2 19950606
US 1995-580567 B2 19951229
US 1996-12299P P 19960226
US 1996-606624 A 19960226
WO 1996-US2882 W 19960226
US 1996-653034 A 19960524
US 1996-701942 A 19960823
US 1996-702308 A 19960823
WO 1997-US14813 W 19970822
US 1999-242119 A3 19990428

OTHER SOURCE(S): MARPAT 131:228949
GI



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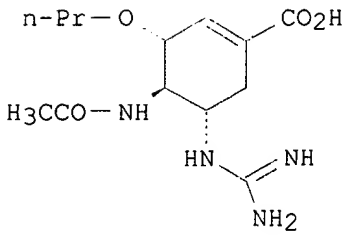

II

AB Amino acid cyclitols I (E = CO2H, ester; G = substituted amine; T = amide; U = alkoxy, thioalkyl, alkylamine) were prepd. as virucides. Methods of inhibiting neuraminidase in samples suspected of contg. neuraminidase are also described. Antigenic materials, polymers, antibodies, conjugates of the compds. of the invention with labels, and assay methods for detecting neuraminidase activity are also described. Thus, cyclitol II.TFA was prepd. and tested for its antiviral activity against influenza.

IT **221386-93-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino acid cyclitols as influenza antiviral agents and neuraminidase inhibitors)

IT **76985-84-7P 187226-87-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid cyclitols as influenza antiviral agents and neuraminidase inhibitors)

REFERENCE COUNT: 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:404916 HCAPLUS
DOCUMENT NUMBER: 131:44605
TITLE: Preparation of cyclohexenecarboxylates as neuraminidase inhibitors
INVENTOR(S): Kim, Choung U.; Lew, Willard
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931047	A1	19990624	WO 1998-US26327	19981210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 477783	B	20020301	TW 1998-87120362	19981208
TW 480247	B	20020321	TW 2001-90111328	19981208
ZA 9811314	A	19990614	ZA 1998-11314	19981210
CA 2313638	AA	19990624	CA 1998-2313638	19981210
AU 9917226	A1	19990705	AU 1999-17226	19981210
US 6111132	A	20000829	US 1998-208646	19981210

EP 1040095	A1	20001004	EP 1998-962059	19981210
EP 1040095	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002508347	T2	20020319	JP 2000-538977	19981210
AT 237582	E	20030515	AT 1998-962059	19981210
ES 2196636	T3	20031216	ES 1998-962059	19981210
HK 1033932	A1	20031010	HK 2001-102443	20010404

PRIORITY APPLN. INFO.: US 1997-69553P P 19971212
WO 1998-US26327 W 19981210

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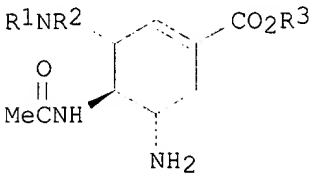


I

AB The title compds. I [R1, R2,, and R3 as defined], neuraminidase inhibitors, were prepd. E.g., I (R1 = H, R2 = CHEt2, R3 = K) was prepd.

IT **182367-90-4P 227599-99-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclohexenecarboxylates as neuraminidase inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:346539 HCAPLUS
DOCUMENT NUMBER: 131:199546
TITLE: Chemoenzymatic Synthesis of Isotopically Labeled Chorismic Acids
AUTHOR(S): Gustin, Darin J.; Hilvert, Donald
CORPORATE SOURCE: Department of Chemistry, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Organic Chemistry (1999), 64(13), 4935-4938
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have prepd. (doubly) labeled chorismic acids via a flexible chemoenzymic route involving the chem. synthesis of shikimate esters followed by enzymic conversion to chorismic acid using an engineered chorismate mutase-deficient E. coli strain.

IT **241465-24-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chemoenzymic synthesis of isotopically labeled chorismic acids)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:216889 HCAPLUS
DOCUMENT NUMBER: 130:237807
TITLE: Preparation of antiviral unsaturated aminodeoxy cyclitols as neuraminidase inhibitors
INVENTOR(S): Bischofberger, Norbert W.; Dahl, Terrence C.;

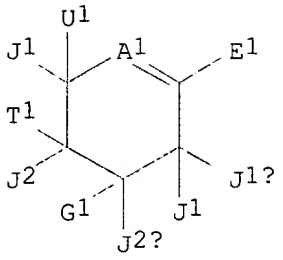
Hitchcock, Michael J. M.; Kim, Choung U.; Lew, Willard; Liu, Hongtao; Mills, Roger G.; Williams, Matthew A.

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 390 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9914185	A1	19990325	WO 1998-US19355	19980915
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2303323	AA	19990325	CA 1998-2303323	19980915
AU 9895694	A1	19990405	AU 1998-95694	19980915
AU 747702	B2	20020516		
EP 1015417	A1	20000705	EP 1998-949356	19980915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9812649	A	20000822	BR 1998-12649	19980915
JP 2001516739	T2	20011002	JP 2000-511738	19980915
NZ 502988	A	20020828	NZ 1998-502988	19980915
ZA 9808451	A	19990331	ZA 1998-8451	19980916

PRIORITY APPLN. INFO.:
US 1997-59308P P 19970917
US 1997-60195P P 19970926
US 1997-938644 A 19970926
WO 1998-US19355 W 19980915

OTHER SOURCE(S): MARPAT 130:237807
GI



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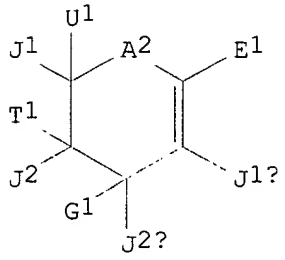
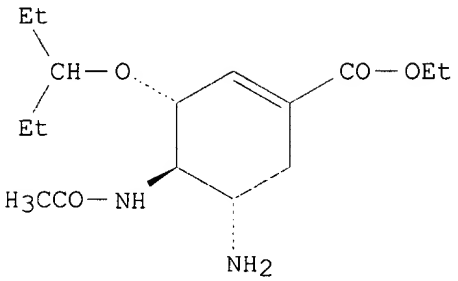


II



III

AB Unsatd. aminodeoxy cyclitols I and II [A1 = CJ1, n, NO; A2 = C(J1)2, NJ1, NOJ1, S, SO, SO2, O; E1 = substituted alkyl, ester; G1 = NH2, N3, CN, OH, alkoxy, NO2, substituted alkyl; T1 = amine, H, acyl amide, halo, CN, nitro, alkoxy, sulfonyl; U1 = H, acyl amide, halo, CN, nitro, alkoxy, sulfonyl; J1, J1a = independently H, alkyl, halo, CN, NO2, N3; J2, J2a = independently H, alkyl] were prepd. as neuraminidase inhibitors. The compds. generally comprise an acidic group, a basic group, a substituted amino or N-acyl and a group having an optionally hydroxylated alkane moiety. Methods of inhibiting neuraminidase in samples suspected of contg. neuraminidase are also described. Antigenic materials, polymers, antibodies, conjugates of the compds. of the invention with labels, and assay methods for detecting neuraminidase activity are also described. Thus cyclitol III was prepd. and tested for its inhibition of neuraminidase.

IT **221386-93-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of antiviral unsatd. aminodeoxy cyclitols as neuraminidase inhibitors)

IT **76985-84-7P 187226-87-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antiviral unsatd. aminodeoxy cyclitols as neuraminidase inhibitors)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:90319 HCAPLUS
DOCUMENT NUMBER: 130:153408
TITLE: Aminocyclohexenecarboxylates as neuraminidase inhibitors
INVENTOR(S): Lew, Willard; Kim, Choung U.; Liu, Hongtao; Williams, Matthew A.
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 395,245,

abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5866601	A	19990202	US 1995-476946	19950606
CA 2188835	AA	19960906	CA 1996-2188835	19960226
WO 9626933	A1	19960906	WO 1996-US2882	19960226
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9653571	A1	19960918	AU 1996-53571	19960226
AU 720933	B2	20000615		
EP 759917	A1	19970305	EP 1996-912404	19960226
EP 759917	B1	20000412		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1147813	A	19970416	CN 1996-190133	19960226
BR 9607098	A	19971104	BR 1996-7098	19960226
JP 11501908	T2	19990216	JP 1996-526442	19960226
JP 3300365	B2	20020708		
US 5952375	A	19990914	US 1996-606624	19960226
EP 976734	A2	20000202	EP 1999-117934	19960226
EP 976734	A3	20000322		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 191711	E	20000415	AT 1996-912404	19960226
ES 2118674	T3	20000816	ES 1996-912404	19960226
PT 759917	T	20001031	PT 1996-96912404	19960226
RU 2181357	C2	20020420	RU 1997-116714	19960226
JP 2002161074	A2	20020604	JP 2001-255372	19960226
NO 9703908	A	19971027	NO 1997-3908	19970826
US 6225341	B1	20010501	US 1999-288091	19990408
GR 3033914	T3	20001130	GR 2000-401599	20000707
US 2002058823	A1	20020516	US 2000-740504	20001219
CN 1347693	A	20020508	CN 2001-124714	20010727

PRIORITY APPLN. INFO.:

US 1995-395245	B2	19950227
US 1995-476946	A	19950606
US 1995-580567	A	19951229
EP 1996-912404	A3	19960226
JP 1996-526442	A3	19960226
US 1996-606624	A3	19960226
WO 1996-US2882	W	19960226
US 1996-653034	A2	19960524
US 1996-701942	A	19960823
US 1996-702308	A	19960823
WO 1997-US14813	W	19970822
US 1999-242119	A3	19990428

OTHER SOURCE(S): MARPAT 130:153408
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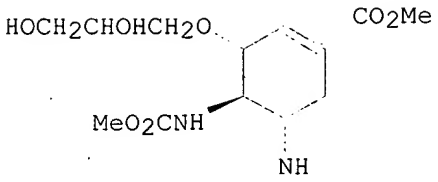


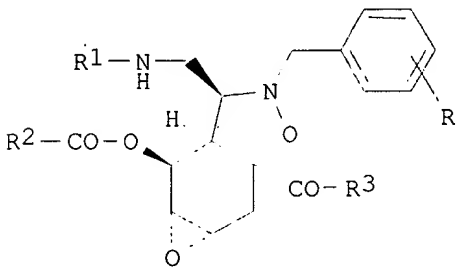
I

AB Novel aminocyclohexenecarboxylates, such as I, are described. The compds. generally comprise an acidic group, a basic group, a substituted amino or N-acyl and a group having an optionally hydroxylated alkane moiety. Pharmaceutical compns. comprising the inhibitors of the invention are also described. Methods of inhibiting neuraminidase in samples suspected of contg. neuraminidase are also described. Antigenic materials, polymers, antibodies, conjugates of the compds. of the invention with labels, and assay methods for detecting neuraminidase activity are also described.

IT **76985-85-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reactant for prepn. of aminocyclohexenecarboxylates as neuraminidase inhibitors)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:503326 HCAPLUS
DOCUMENT NUMBER: 129:244668
TITLE: Stereoselective Synthesis of over Two Million Compounds Having Structural Features Both Reminiscent of Natural Products and Compatible with Miniaturized Cell-Based Assays
AUTHOR(S): Tan, Derek S.; Foley, Michael A.; Shair, Matthew D.; Schreiber, Stuart L.
CORPORATE SOURCE: Department of Chemistry Chemical Biology Harvard Institute of Chemistry Cell Biology, Howard Hughes Medical Institute Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (1998), 120(33), 8565-8566
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:244668
GI



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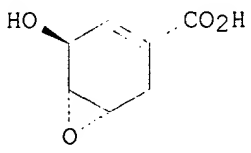


II

AB A combinatorial library of 2.18 million octahydrobenzoisoxazoles I (R = 2-I, 3-I, 4-I, 2-R4C.tplbond.C, 3-R4C.tplbond.C, 4-R4C.tplbond.C; R1 = alkyl, cycloalkyl, arylalkyl; R2 = alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl; R3 = NH2, CH2CONH2, (CH2)5CONH2; R4 = alkyl, aryl, arylalkyl) has been generated to give a set rigid, stereochem. defined, and structurally diverse mols. The libraries are prepd. in six steps from either enantiomer of oxacycloheptane II by linking to a solid support with one of three linkers, esterification and dipolar cycloaddn. with arylmethyl glycine nitrones, Sonogashira coupling of the product iodoaryl derivs. with alkynes, lactone cleavage with amines, acylation of the free alcs. with acids and acyl coupling reagents, and photochem. cleavage from the resin. Sublibraries of I were prepd. to test the reactivity of alkynes, amines, and acids in the preparative sequence towards I and the purity of the products generated. Libraries generated by this sequence are spatially sepd. and encoded, allowing for controlled release of libraries into soln. and for cell-based testing of the libraries.

IT **76985-84-7 106861-60-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of starting materials for a combinatorial library of rigid, stereochem. defined compds.)

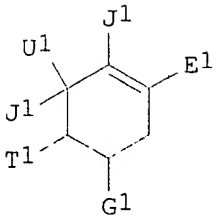
IT **206537-16-8P 213027-96-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of starting materials for a combinatorial library of rigid, stereochem. defined compds.)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:397793 HCAPLUS
DOCUMENT NUMBER: 129:54135
TITLE: Preparation of aminocyclohexenylcarboxylates and related compounds as neuraminidase inhibitors.
INVENTOR(S): Bischofberger, Norbert W.; Kim, Choung U.; Lew, Willard; Liu, Hongtao; Williams, Matthew A.
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: U.S., 74 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763483	A	19980609	US 1996-774345	19961227

PRIORITY APPLN. INFO.: US 1996-774345 19961227
OTHER SOURCE(S): MARPAT 129:54135
GI



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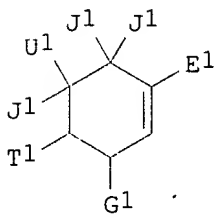
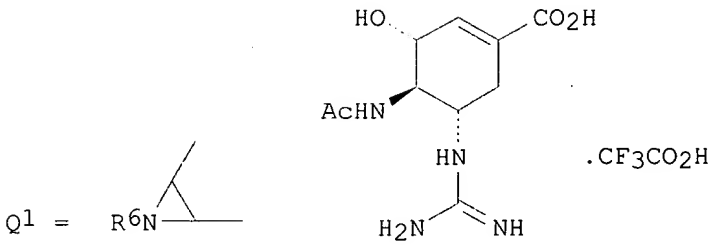


II



III

AB Title compds. [I, II; E1 = [(CR1)2]mW1; W1 = group comprising an acidic H, protected acidic group, etc.; G1 = N3, CN, OH, OR5, NO2, [(CR1)2]mW2; R5 = H, protecting group; W2 = group comprising a basic heteroatom, etc.; T1 = NR1W3, heterocyclyl; W3 = (substituted) alkyl, alkenyl, alkynyl, acyl, heterocyclyl, etc.; T1U1 or T1G1 = Q1; U1 = H, X1W6; X1 = bond, O, imino, S, SO, SO2, etc.; W6 = (substituted) alkyl, alkenyl, alkynyl, acyl, amino, aminocarbonyl, etc.; J1 = H, F, Cl; R1 = H, alkyl; R6 = H, protecting group, residue of carboxyl-contg. compd.; m = 0-2; with provisos], were prepd. Thus, title compd. (III) (prepn. given) inhibited neuraminidase with IC50 <1.0 .mu.M.

IT **76985-84-7P 187226-87-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aminocyclohexenylcarboxylates and related compds. as neuraminidase inhibitors)

REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:251317 HCAPLUS
DOCUMENT NUMBER: 128:319046
TITLE: Droplet assay system for screening combinatorial libraries
INVENTOR(S): Schreiber, Stuart L.; Shair, Matthew D.; Borchardt, Allen J.; You, Angie J.; Huang, Jing; Foley, Mike; Tan, Derek; Whitesides, George; Jackman, Rebecca J.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816830	A2	19980423	WO 1997-US19110	19971015

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9852391 A1 19980511 AU 1998-52391 19971015
PRIORITY APPLN. INFO.: US 1996-29128P P 19961016
US 1997-49864P P 19970606
WO 1997-US19110 W 19971015

AB The present invention provides a novel system for simultaneously screening a large no. of compds. and identifying compds. having desirable chem. or biol. activities. According to the invention, test compds. are isolated in and introduced into liq. droplets within which their activities are studied. Multiple droplets are displayed simultaneously on a single surface without risk of confusion because the sep. identity of each droplet is maintained and diffusion of test compds. from one droplet to another is avoided. In certain embodiments, these goals are accomplished through reliance on droplet surface tension. In other embodiments, the droplets are localized in micro-wells that retain droplet integrity. The system is particularly useful for identifying compds. that act e.g., as catalysts, or that have biol. activities. In preferred embodiments of the invention, the compds. are assayed in vivo.

IT **76985-84-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(droplet assay system for simultaneously assaying combinatorial libraries and identifying compds. of chem. or biol. activities)

IT **206537-16-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(droplet assay system for simultaneously assaying combinatorial libraries and identifying compds. of chem. or biol. activities)

L12 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:36607 HCAPLUS
DOCUMENT NUMBER: 128:61662
TITLE: Total Synthesis of (+)-Narciclasine
AUTHOR(S): Rigby, James H.; Mateo, Mary E.
CORPORATE SOURCE: Department of Chemistry, Wayne State University, Detroit, MI, 48202-3489, USA
SOURCE: Journal of the American Chemical Society (1997), 119(51), 12655-12656
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:61662
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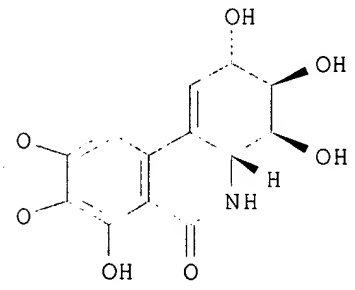

I

AB The anticancer amaryllidaceae alkaloid, (+)-narciclasine (I) was synthesized in enantiomerically pure form. Construction of the

phenanthridone ring system features a novel hydrogen-bond controlled aryl enamide photocyclization. Subsequent dehydration of the C1 hydroxyl group and routine functional group manipulation afforded the target mol.

IT **200182-30-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (+)-narciclasine)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:703177 HCAPLUS
DOCUMENT NUMBER: 127:331672
TITLE: Influenza neuraminidase inhibitors possessing a novel hydrophobic interaction in the enzyme active site: design, synthesis, and structural analysis of carbocyclic sialic acid analogs with potent anti-influenza activity
AUTHOR(S): Rotella, David P.
CORPORATE SOURCE: Bristol-Myers Squibb, USA
SOURCE: Chemtracts (1997), 10(11), 836-840
CODEN: CHEMFW; ISSN: 1431-9268
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two novel carbocyclic analogs of sialic acid are prepd. for study as potential inhibitors of neuraminidase, a crit. enzyme in influenza virus replication. The syntheses begin with either (-)-shikimic acid or (-)-quinic acid, and involve sequential formation and opening of aziridine rings to create the key diamino moiety. Ether analogs of the target compd. were found to be potent virucides, and one ether (GS4104) was put into development for oral treatment and prophylaxis of influenza infection.

IT **149560-23-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis, and structural anal. of carbocyclic sialic acid analogs with potent anti-influenza activity)

L12 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:21109 HCAPLUS
DOCUMENT NUMBER: 126:171813
TITLE: Influenza Neuraminidase Inhibitors Possessing a Novel Hydrophobic Interaction in the Enzyme Active Site: Design, Synthesis, and Structural Analysis of Carbocyclic Sialic Acid Analogs with Potent Anti-Influenza Activity
AUTHOR(S): Kim, Choung U.; Lew, Willard; Williams, Matthew A.; Zhang, Lijun; Liu, Hongtao; Swaminathan, S.; Bischofberger, Norbert; Chen, Ming S.; Tai, Chun Y.; Mendel, Dirk B.; Laver, W. Graeme; Stevens, Raymond C.
CORPORATE SOURCE: Gilead Sciences Inc., Foster City, CA, 94404, USA
SOURCE: Journal of the American Chemical Society (1997), 119(4), 681-690
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
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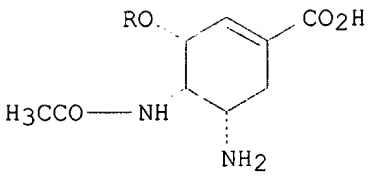

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AB The design, synthesis, and in vitro evaluation of the novel carbocycles as transition-state-based inhibitors of influenza neuraminidase (NA) are described. The double bond position in the carbocyclic analogs plays an important role in NA inhibition as demonstrated by the antiviral activity of 8 (IC50 = 6.3 .mu.M) vs 9 (IC50 > 200 .mu.M). Structure-activity studies of a series of carbocyclic analogs, e.g. I (R = H, Me, Et, Pr, Bu), identified the 3-pentyloxy moiety as an apparent optimal group at the C3 position with an IC50 value of 1 nM for NA inhibition. The X-ray crystallog. structure of 6h bound to NA revealed the presence of a large hydrophobic pocket in the region corresponding to the glycerol subsite of sialic acid. The high antiviral potency obsd. for 6h appears to be attributed to a highly favorable hydrophobic interaction in this pocket. The practical prepn. of I starting from (-)-quinic acid is also described.

IT **76985-84-7P 187226-87-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of carbocyclic sialic acid analogs with potent influenza activity)

L12 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:637103 HCAPLUS
DOCUMENT NUMBER: 125:300503
TITLE: Preparation of selective inhibitors of viral or bacterial neuraminidases
INVENTOR(S): Bischofberger, Norbert W.; Kim, Choung U.; Lew, Willard; Liu, Hongtao; Williams, Matthew A.
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 345 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9626933	A1	19960906	WO 1996-US2882	19960226
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5866601	A	19990202	US 1995-476946	19950606
AU 9653571	A1	19960918	AU 1996-53571	19960226
AU 720933	B2	20000615		
EP 759917	A1	19970305	EP 1996-912404	19960226
EP 759917	B1	20000412		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9607098	A	19971104	BR 1996-7098	19960226
JP 11501908	T2	19990216	JP 1996-526442	19960226
JP 3300365	B2	20020708		
AT 191711	E	20000415	AT 1996-912404	19960226

RU 2181357	C2	20020420	RU 1997-116714		19960226
TW 426663	B	20010321	TW 1996-85107487		19960621
NO 9703908	A	19971027	NO 1997-3908		19970826
GR 3033914	T3	20001130	GR 2000-401599		20000707
PRIORITY APPLN. INFO.:			US 1995-395245	A	19950227
			US 1995-476946	A	19950606
			US 1995-580567	A	19951229
			US 1996-12299P	P	19960226
			US 1996-606624	A	19960226
			WO 1996-US2882	W	19960226
			US 1996-653034	A	19960524

OTHER SOURCE(S): MARPAT 125:300503

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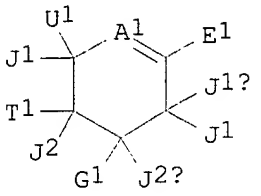

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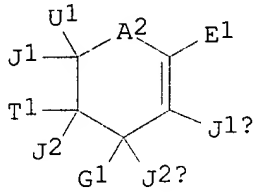

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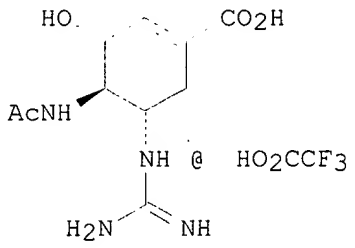

III

AB The title compds. [I, II; A1 = (un)substituted CH, N; A2 = (un)substituted CH2, (un)substituted NH, N(O), S, SO, SO2, O; E1 = terminal-(un)substituted alkyl; G1 = N3, CN, OH, NO2, alkoxy, etc.; T1 = (un)substituted NH2, heterocyclyl; J1, J1a = H, alkyl, halogen, CN, NO2, N3, etc.; U1 = H, (un)substituted SO3H, etc.; J2, J2a = H, alkyl] (e.g., III; IC50 <1.0 .mu.M), useful as selective inhibitors of viral or bacterial neuraminidases, are prepd.

IT **76985-85-8P 182367-90-4P 182368-11-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of selective inhibitors of viral or bacterial neuraminidases)

L12 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1996:446722 HCAPLUS
DOCUMENT NUMBER:	125:107953
TITLE:	Biosynthesis of 3-amino-5-hydroxybenzoic acid, the precursor of mC7N units in ansamycin antibiotics
AUTHOR(S):	Kim, Chun-Gyu; Kirschning, Andreas; Bergon, Phillipe; Zou, Pei; Su, Ester; Sauerbrei, Bernd; Ning, Sandra; Ahn, Yonghyun; Breuer, Michael; et al.
CORPORATE SOURCE:	Department of Chemistry, University of Washington, Seattle, WA, 98195-1700, USA
SOURCE:	Journal of the American Chemical Society (1996), 118(32), 7486-7491 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

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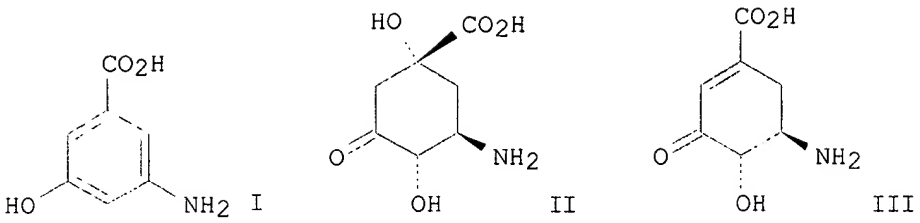

AB The biosynthetic pathway of 3-amino-5-hydroxybenzoic acid (I) formation was studied with cell-free exts. from the rifamycin B producer Amycolatopsis mediterranei S699 and the ansatrienin A producer Streptomyces collinus Tu1892. Phosphoenolpyruvate (PEP) plus erythrose 4-phosphate (E4P) gave AHBA in low but nevertheless significant (6%) yield. 3,4-Dideoxy-4-amino-D-arabino-heptulosonic acid 7-phosphate (aminoDAHP) was converted efficiently into I (45%), as were 5-deoxy-5-amino-3-dehydroquinic acid (II, 41%) and 5-deoxy-5-amino-3-dehydroshikimic acid (III, 95%). On the other hand, the normal shikimate pathway intermediate 3-deoxy-D-arabino-heptulosonic acid 7-phosphate (DAHP) did not give rise to I under these conditions. AminoDAHP (9%) was produced by incubation of [14C]PEP and E4P, but not of [14C]DAHP, with the cell-free exts. The results demonstrate the operation of a new variant of the shikimate pathway in the formation of the mC7N units of ansamycin, and presumably also mitomycin, antibiotics which leads from PEP, E4P, and a nitrogen source directly to aminoDAHP and then via II and III to I.

IT **76985-84-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(regiospecific ring cleavage of)

L12 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:368765 HCAPLUS
DOCUMENT NUMBER: 125:143175
TITLE: Synthesis of (3R)- and (3S)-fluoro-(4R,5R)-dihydroxy-1-cyclohexene-1-carboxylic acids: the (3R)- and (3S)-fluoro analogs of (-)-shikimic acid
AUTHOR(S): Brettle, Roger; Cross, Richard; Frederickson, Martyn; Haslam, Edwin; MacBeath, Fiona S.; Davies, Gareth M.
CORPORATE SOURCE: Dep. Chem., Univ. Sheffield, Sheffield, S3 7HF, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(11), 1275-1278
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB (3R)- and (3S)-Fluoro-(4R,5R)-dihydroxy-1-cyclohexene-1-carboxylic acids (the (3R)- and (3S)-fluoro analogs of (-)-shikimic acid) have been synthesized from (-)-shikimic acid via an intermediate epoxide (a fungal metabolite from chalara microspora) that underwent acid catalyzed hydrolysis to afford the first stereospecific synthesis of (-)-3-epi-shikimic acid.

IT **106861-60-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of fluorodihydroxycyclohexenecarboxylic acids)

L12 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:156905 HCAPLUS
DOCUMENT NUMBER: 124:224827
TITLE: An EPSP Synthase Inhibitor Joining Shikimate 3-Phosphate with Glyphosate: Synthesis and Ligand Binding Studies
AUTHOR(S): Marzabadi, Mohammad R.; Gruys, Kenneth J.; Pansegrau, Paul D.; Walker, Mark C.; Yuen, Henry K.; Sikorski, James A.
CORPORATE SOURCE: Ceregen Unit, Monsanto Company, St. Louis, MO, 63198, USA
SOURCE: Biochemistry (1996), 35(13), 4199-210
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
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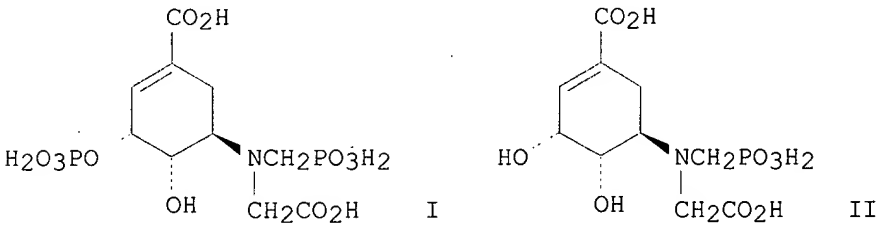

AB A novel EPSP synthase inhibitor I has been designed and synthesized to probe the configurational details of glyphosate recognition in its herbicidal ternary complex with enzyme and shikimate 3-phosphate (S3P). A kinetic evaluation of the new 3-dephospho analog II, as well as calorimetric and 31P NMR spectroscopic studies of enzyme-bound I, now provides a more precise quant. definition for the mol. interactions of I with this enzyme. The very poor binding, relative to I, displayed by the 3-dephospho analog II is indicative that I has a specific interaction with the S3P site. A comparison of Ki(calc) for II vs. the Ki(app) for I indicates that the 3-phosphate group in I contributes about 4.8 kcal/mol to binding. This compares well with the 5.2 kcal/mol which the 3-phosphate group in S3P contributes to binding. Isothermal titrn. calorimetry demonstrates that I binds to free enzyme with an obsd. Kd of 0.53 .mu.M. As such, I binds only 3-fold weaker than glyphosate and about 150-fold better than N-methylglyphosate. Consequently, I represents the most potent N-alkylglyphosate deriv. identified to date. However, the resulting thermodn. binding parameters clearly demonstrate that the formation of EPSPS.cntdot.I is entropy driven like S3P. The binding characteristics of I are fully consistent with a primary interaction localized at the S3P subsite. Furthermore, 31P NMR studies of enzyme-bound I confirm the expected interaction at the shikimate 3-phosphate site. However, the chem. shift obsd. for the phosphonate signal of EPSPS.cntdot.I is in the opposite direction than that obsd. previously when glyphosate binds with enzyme and S3P. Therefore, when I occupies the S3P binding site, there is incomplete overlap at the glyphosate phosphonate subsite. As a glyphosate analog inhibitor, the potency of I most likely arises from predominant interactions which occur outside the normal glyphosate binding site. Consequently, I is best described as an S3P-based substrate-analog inhibitor. These combined results corroborate the previous kinetic model [Gruys, K. J., Marzabadi, M. R., Pansegrau, P. D., & Sikorski, J. A. (1993) Arch. Biochem. Biophys. 304, 345-351], which suggested that I interacts well with the S3P subsite but has little, if any, interaction at the expected glyphosate phosphonate or phosphoenolpyruvate-Pi subsites.

IT **76985-84-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(EPSP synthase inhibitor joining shikimate 3-phosphate with glyphosate, its synthesis and ligand binding studies)

L12 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:937582 HCAPLUS
DOCUMENT NUMBER: 124:25613
TITLE: Chemical constituents of dayecai (Selaginella doederleinii)
AUTHOR(S): Chen, Ping; Sun, Jingyun; Xie, Niangeng; Shi, Yingu
CORPORATE SOURCE: Zhejiang Acad. Traditional Chinese Medicine Materia Medica, Hangzhou, 310007, Peop. Rep. China
SOURCE: Zhongcaoyao (1995), 26(8), 397-9
CODEN: CTYAD8; ISSN: 0253-2670
PUBLISHER: Guojia Yiyao Guanliju Tianjin Yaowu Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
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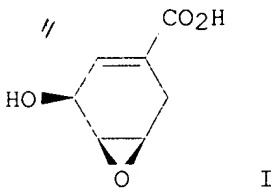

I

AB Five compds. isolated from the herb of S. doederleinii Hiero were identified as doederleinic acid (I), apigenin, isopimpinellin, .beta.-sitosterol and stearic acid resp. on the basis of phys. and chem. properties and spectra data. I is a new natural product, while the others were all isolated for the 1st time from this plant.
IT **171596-14-8P**, Doederleinic acid
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(chem. constituents of Selaginella doederleinii)

L12 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:539650 HCAPLUS
DOCUMENT NUMBER: 119:139650
TITLE: Design & synthesis of a novel EPSP synthase inhibitor based on its ternary complex with shikimate-3-phosphate and glyphosate
AUTHOR(S): Marzabadi, Mohammad R.; Font, Jose L.; Gruys, Kenneth J.; Pansegrau, Paul D.; Sikorski, James A.
CORPORATE SOURCE: New Prod. Div., Units Monsanto Co., St. Louis, MO, 63198, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1992), 2(11), 1435-40
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
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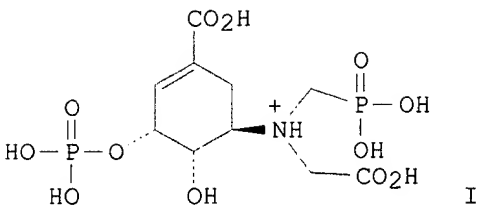

I

AB A novel EPSP (5-enolpyruvoyl-shikimate-3-phosphate) synthase inhibitor I has been designed and synthesized to define the conformational and configurational details of glyphosate recognition in its herbicidal ternary complex with enzyme and shikimate-3-phosphate (S3P).

IT **149560-23-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in synthesis of shikimate phosphate)

L12 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:41162 HCAPLUS
DOCUMENT NUMBER: 116:41162
TITLE: Phosphonate analogs of chorismic acid: synthesis and evaluation as mechanism-based inactivators of chorismate mutase
AUTHOR(S): Wood, Harold B.; Buser, Hans Peter; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Journal of Organic Chemistry (1992), 57(1), 178-84
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
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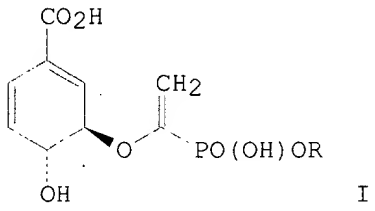

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AB Two potential mechanism-based mutase inactivators, phosphonochorismic acids I (R = H, Me), were prepd. utilizing new transition-metal-catalyzed insertion reactions of tetraalkyl diazophosphonates. Thermolysis of I in the absence of enzyme led to 4-HOC6H4CO2H, with no trace of the expected Claisen rearrangement product. When tested over a wide range of concns. against the E. coli chorismate mutases (so-called T- and P-proteins), neither I interacted with the enzyme, either as a competitive inhibitor or as a substrate, perhaps reflecting the stringent demands of the rearrangement transition state. Earlier studies strongly suggest that the enol pyruvate carboxyl group is markedly tilted against the carbocyclic ring during [3,3] sigmatropy, and similar flattening of the tetrahedral phosphonate could create unfavorable steric as well as .pi.-.pi. interactions.

IT **106861-60-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(rhodium-catalyzed insertion reaction of, with diphosphonodiazomethane)

L12 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:492775 HCAPLUS
DOCUMENT NUMBER: 115:92775

TITLE: Synthesis and evaluation of two new inhibitors of EPSP synthase
AUTHOR(S): Pansegrau, Paul D.; Anderson, Karen S.; Widlanski, Theodore; Ream, Joel E.; Sammons, R. Douglas; Sikorski, James A.; Knowles, Jeremy R.
CORPORATE SOURCE: Tech. Div., Monsanto Agric. Co., St. Louis, MO, 63167, USA
SOURCE: Tetrahedron Letters (1991), 32(23), 2589-92
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:92775
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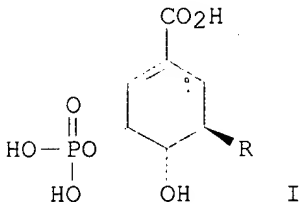

I

AB The enzyme EPSP synthase, EPSPS, (EC 2.5.1.19) catalyzes an unusual transfer reaction of the enolpyruvoyl moiety from phosphoenol pyruvate regiospecifically to the 5-OH of shikimate 3-phosphate I (R = OH) (II) to form 5-enol-pyruvoylshikimate 3-phosphate I [R = C(CH2)CO2H]. Two new inhibitors I (R = H, NH2) were prepd. to prove the II binding site.
IT **76985-84-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., bromination, and azidolysis of)

L12 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:159625 HCAPLUS
DOCUMENT NUMBER: 114:159625
TITLE: A rule to predict which enantiomer of a secondary alcohol reacts faster in reactions catalyzed by cholesterol esterase, lipase from Pseudomonas cepacia, and lipase from Candida rugosa
AUTHOR(S): Kazlauskas, Romas J.; Weissfloch, Alexandra N. E.; Rappaport, Aviva T.; Cuccia, Louis A.
CORPORATE SOURCE: Dep. Chem., McGill Univ., Montreal, QC, H3A 2K6, Can.
SOURCE: Journal of Organic Chemistry (1991), 56(8), 2656-65
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The enantioselectivity of the title enzymes for more than 130 esters of secondary alcs. is correlated by a rule based on the sizes of the substituents at the stereocenter. This rule predicts which enantiomer of a racemic secondary alc. reacts faster for 14 of 15 substrates of cholesterol esterase (CE), 63 of 64 substrates of lipase from P. cepacia (PCL), and 51 of 55 cyclic substrates of lipase from C. rugosa (CRL). The enantioselectivity of CRL for acyclic secondary alcs. is not reliably predicted by this rule. This rule implies that the most efficiently resolved substrates are those having substituents which differ significantly in size. This hypothesis was used to design syntheses of 2 chiral synthons: esters of (R)-lactic acid and (S)-(-)-4-acetoxy-2-cyclohexen-1-one (I). As predicted, the acetate group of the Me ester of lactyl acetate was hydrolyzed by PCL with low enantioselectivity because the 2 substituents, CH3 and C(O)OCH3, are similar in size. To improve the

enantioselectivity, the Me ester was replaced by a tert-Bu ester. The acetate group of the tert-Bu ester of lactyl acetate was hydrolyzed with high enantioselectivity (E >50). Enantiomerically pure (R)-(+)-tert-Bu lactate (>98% ee, 6.4 g) was prepd. by kinetic resoln. For the 2nd example, low enantioselectivity (E <3) was obsd. in the hydrolysis of cis-1,4-diacetoxycyclohex-2-ene, a meso substrate where the 2 substituents, CH2CH2 and CH:CH, are similar in size. To improve enantioselectivity, the size of the CH:CH substituent was increased by addn. of Br2. The new substrate was hydrolyzed with high enantioselectivity (E >65) using either CE or CRL. Enantiomerically pure I (98% ee) was obtained after removal of the bromines with Zn and oxidn. with CrO3/pyridine.

IT **106861-59-0 106861-61-4**
RL: BIOL (Biological study)
(cholesterol esterase of pancreas and lipase of Candida rugosa enantiospecificity for, rule for prediction of, structure in relation to)

L12 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:23661 HCAPLUS
DOCUMENT NUMBER: 114:23661
TITLE: Short chemical synthesis of (-)-chorismic acid from (-)-shikimic acid
AUTHOR(S): Wood, Harold Blair; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Journal of the American Chemical Society (1990), 112(24), 8907-9
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:23661
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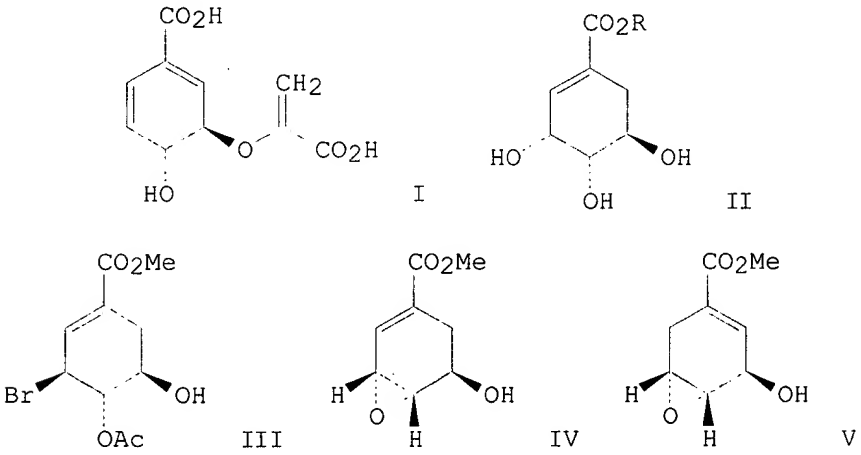

AB A short and efficient partial synthesis of (-)-chorismic acid (I) from (-)-shikimic acid (II; R = H) is reported. Chorismate is the key branch-point intermediate in the shikimic acid pathway, which bacteria, fungi, and lower plants use to biosynthesize inter alia the amino acids phenylalanine, tyrosine, and tryptophan as well as the isoprenoid quinones and folate coenzymes. Reaction of (-)-Me shikimate (II; R = Me) with 2-acetoxyisobutyryl bromide (MeCN, 0.degree., 30 min) afforded (+)-Me (3R,4S,5R)-3-bromo-4-acetoxy-5-hydroxy-1-cyclohexene-1-carboxylate (III)

in 76-85% yield. Transesterification of this bromoacetate with NaOMe (1.05 equiv, MeOH, 0.degree., 30 min) led quant. to the corresponding epoxyol, (+)-Me 3,4-anhydroshikimate (IV). Payne rearrangement of this trans epoxyol (NaOMe-MeOH, 50.degree., 10 min) produced (-)-Me (3S,4S,5R)-3-hydroxy-4,5-epoxy-1-cyclohexene-1-carboxylate (V), which has previously been converted into (-)-chorismic acid. This shikimate to chorismate transformation constitutes the first synthetic interconversion paralleling the biogenetic relationship shared by these two metabolites.

IT **76985-84-7P**
RL: SPN (Synthetic preparation); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in prepn. of chorismic acid intermediate)

IT **106861-60-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as key chorismic acid intermediate)

L12 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:454938 HCAPLUS
DOCUMENT NUMBER: 113:54938
TITLE: Mechanistic studies on trans-2,3-dihydro-2,3-dihydroxybenzoate dehydrogenase (Ent A) in the biosynthesis of the iron chelator enterobactin
AUTHOR(S): Sakaitani, Masahiro; Rusnak, Frank; Quinn, Nina R.; Tu, Cheng; Frigo, Timothy B.; Berchtold, Glenn A.; Walsh, Christopher T.
CORPORATE SOURCE: Dep. Biol. Chem. Mol. Pharmacol., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Biochemistry (1990), 29(29), 6789-98
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2,3-Dihydro-2,3-dihydroxybenzoate dehydrogenase (I), the product of the enterobactin biosynthetic gene entA, catalyzes the NAD-dependent oxidn. of the dihydroarom. substrate 2,3-dihydro-2,3-dihydroxybenzoate (2,3-diDHB) to the arom. catecholic product 2,3-dihydroxybenzoate (2,3-DHB). 2,3-DHB is one of the key siderophore units of enterobactin, a potent Fe chelator secreted by Escherichia coli. To probe the reaction mechanism of this oxidn., a variety of 2,3-diDHB analogs were synthesized and tested as substrates. An attempt was made to elucidate both the regio- and stereospecificity of alc. oxidn. as well as the stereochem. of NAD redn. Of those analogs tested, only those with a C3-hydroxyl group (but not a C2-hydroxyl group) were oxidized to the corresponding ketone products. The reversibility of the I-catalyzed reaction was demonstrated with the corresponding NADH-dependent redn. of 3-ketocyclohexane- and -cyclohexene-1-carboxylates but not the 2-keto compds. The results established that I functions as an alc. dehydrogenase to specifically oxidize the C3-hydroxyl group of 2,3-diDHB to produce the corresponding 2-hydroxy-3-oxo-4,6-cyclohexadiene-1-carboxylate as a transient species that undergoes rapid aromatization to give 2,3-DHB. The stereospecificity of the C3 allylic alc. group oxidn. was confirmed to be 3R in a 1R,3R dihydro substrate and hydride transfer occurred to the si face of enzyme-bound NAD.

IT **106861-61-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)

IT **127943-88-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dihydrodihydroxybenzoate dehydrogenase of Escherichia coli response to, structure in relation to)

IT **76947-23-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(sapon. of)

L12 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:423496 HCAPLUS
DOCUMENT NUMBER: 113:23496
TITLE: The structure of naturally-occurring (+)-methyl 3,4-anhydroshikimate
AUTHOR(S): Wood, Harold B.; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Tetrahedron Letters (1989), 30(46), 6257-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:23496
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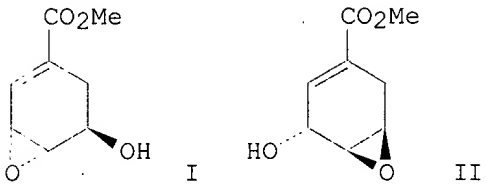

AB Enantiomerically pure (+)-Me 3,4-anhydroshikimate (I) was prepd. from (-)-Me shikimate in 2 steps, and has [.alpha.]D = +248.degree. (c 0.5, EtOH). I rearranged to epoxide II on prolonged contact with MeONa giving a mixt. with [.alpha.]D = +35.degree. (c 0.2, EtOH).
IT **106861-60-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L12 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:188330 HCAPLUS
DOCUMENT NUMBER: 110:188330
TITLE: Structural requirements for catalysis by chorismate mutase
AUTHOR(S): Pawlak, John L.; Padykula, Robert E.; Kronis, John D.; Aleksejczyk, Robert A.; Berchtold, Glenn A.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of the American Chemical Society (1989), 111(9), 3374-81
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
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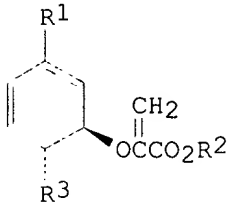
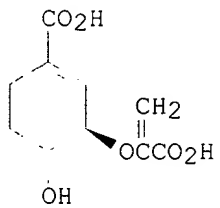


I, $R^1=R^2=H$, $R^3=OH$
II, $R^1=CO_2H$, $R^2=H$, $R^3=OMe$
IV, $R^1=CO_2H$, $R^2=Me$, $R^3=OH$



V

AB The structural requirements for mutase-catalyzed Claisen rearrangement by chorismate mutase-prephenate dehydrogenase from Escherichia coli were established. The chorismate analog (I) lacking the carboxyl group at C1 was not a substrate for chorismate mutase. The chorismate Me ether [(.+-.)-II] was a good substrate for chorismate mutase (kcat/kuncat = 2.0 .times. 104). The half-lives for Claisen rearrangement and aromatization of 4-deshydroxychorismate (III) in D2O at 30.degree., pD 7.2, were 3.5 and 8 min, resp. In the presence of large amts. of enzyme, it was demonstrated that the Claisen rearrangement of enantiomerically pure III was accelerated .gtoreq.100-fold by chorismate mutase. Data available from other studies have demonstrated that ester IV is not a substrate for chorismate mutase, and the kcat/kuncut for dihydrochorismate analog V is similar to that for chorismate. These results establish that the only functional groups required on the allyl vinyl ether moiety of chorismate for mutase-catalyzed rearrangement are the 2 carboxylate groups.

IT **106861-61-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxirane ring opening of, by diphenylselenide)

IT **76985-85-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of)

L12 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:23609 HCAPLUS
DOCUMENT NUMBER: 110:23609
TITLE: Uncatalyzed and chorismate mutase-catalyzed Claisen rearrangement of (Z)-9-methylchorismic acid
AUTHOR(S): Lesuisse, Dominique; Berchtold, Glenn A.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Organic Chemistry (1988), 53(21), 4992-7
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:23609
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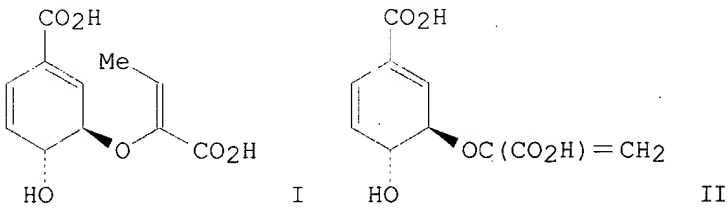

AB A synthesis of (-)- and (.+-.)-(Z)-9-methylchorismic acid (I) is reported. The half-life for the uncatalyzed Claisen rearrangement of (.+-.)-I in H2O (pH 7.5, 360.degree.) is 5.7 h. Chorismate analog (-)-I was a modest substrate for chorismate mutase (chorismate mutase-prephenate dehydrogenase from E. coli): Km = 4.0 mM, kcat./kuncat. = 4.2 .times. 104. The enzyme-catalyzed Claisen rearrangement of (-)-I proceeds through a chairlike transition state in similar fashion to the chorismate mutase-catalyzed rearrangement of (-)-chorismic acid (II).

IT **76947-23-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-alkylation of, by diazophosphonoacetate)

L12 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:473150 HCAPLUS

DOCUMENT NUMBER: 107:73150
TITLE: Chorismate aminations: partial purification of Escherichia coli PABA synthase and mechanistic comparison with anthranilate synthase
AUTHOR(S): Walsh, Christopher T.; Erion, Mark D.; Walts, Alan E.; Delany, John J., III; Berchtold, Glenn A.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Biochemistry (1987), 26(15), 4734-45
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
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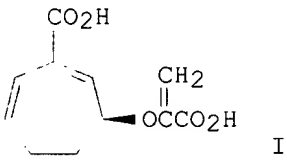

I

AB Chorismate is converted by regiospecific amination/aromatization sequences to o-aminobenzoate and p-PABA by anthranilate synthase (AS) and PABA synthase (PABS), resp. Here, the 1st partial purifn. of the large subunit of Escherichia coli PABA synthase, previously reported to be quant. inactivated in purifn. attempts, is reported. The subunit encoded by the pabB gene was overexpressed from a T7 promoter and purified 9-fold to 25-30% homogeneity. The pabB subunit appears unusually sensitive to inactivation by glycerol, so this cosolvent is contraindicated. The Km for chorismate is 42 .mu.M in the NH3-dependent conversion to PABA, and a turnover no. of 2.6 min-1 is estd. A variety of chorismate analogs were prepd. and examd. Of these compds., a cycloheptadienyl analog (I) has been found to be the most potent inhibitor of Serratia mercescens AS (Ki = 30 .mu.M for an RS mixt.) and of the E. coli pabB subunit of PABA synthase (Ki = 226 .mu.M). Modifications in the substituents at C-3 [enolpyryuyl ether, (R)- or (S)-lactyl ether, glycolyl ether] or C-4 (O-methyl) of chorismate lead to alternate substrates. The Vmax values for (R)- and (S)-lactyl ethers are down 10-20-fold for each enzyme, and Vmax/Km analyses show the (S)-lactyl chorismate analog to be preferred by 12/1 over (R)-lactyl for anthranilate synthase whereas a 3/1 preference was obsd. for (R)-(S)-lactyl analogs by PABA synthase. The glycolyl ether analog of chorismate shows 15% Vmax vs. chorismate for AS but is actually a faster substrate (140%) than chorismate with PABA synthase, suggesting the elimination/aromatization step from an aminocyclohexadienyl species may be rate limiting with AS but not with PABS. Indeed, studies with an (R)-lactyl analog and AS led to accumulation of an intermediate, isolable by HPLC and characterized by NMR and UV-visible spectroscopy as 6-amino-5-[(1-carboxyethyl)oxy]-1,3-cyclohexadiene-1-carboxylic acid (II). This is the anticipated intermediate predicted by previous work with conversion of synthetic trans-6-amino-5-[(1-carboxyethenyl)oxy]-1,3-cyclohexadiene-1-carboxylic acid to anthranilate by the enzyme. II is quant. converted to anthranilate on reincubation with enzyme, but at a 1.3-10-fold lower Vmax than starting lactyl substrate under the conditions investigated; the basis for this kinetic variation is not yet detd.

IT **106861-60-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Me .alpha.-diazopropionate in Rh2 (N-octyl)4 presence)

L12 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:172361 HCAPLUS
DOCUMENT NUMBER: 106:172361
TITLE: Total synthesis of (-)-chorismic acid and (-)-shikimic acid
AUTHOR(S): Pawlak, John L.; Berchtold, Glenn A.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Organic Chemistry (1987), 52(9), 1765-71
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A survey is reported of the enantioselective hydrolyses of esters of Me (1.beta.,2.beta.,6.beta.)-2-hydroxy-7-oxabicyclo[4.1.0]hept-3-ene-4-carboxylate and of Me (1.alpha.,2.beta.,6.alpha.)-2-hydroxy-7-oxabicyclo[4.1.0]hept-3-ene-4-carboxylate (I) with com. available lipases and cholesterol esterases. A procedure for the preparative-scale synthesis of enantiomerically pure (+)- and (-)-Me (1.beta.,2.alpha.,6.beta.)-2-hydroxy-7-oxabicyclo[4.1.0]hept-3-ene-4-carboxylate [(+)- and (-)-(II)] by the enantioselective hydrolysis of the butyric acid or hexanoic acid ester of I with cholesterol esterase from bovine pancreas is described. Enantiomerically pure (-)-Me (1.beta.,2.beta.,6.beta.)-2-hydroxy-7-oxabicyclo[4.1.0]hept-3-ene-4-carboxylate[(-)-(III)] is prepd. from either (+)-II or (-)-II. A short total synthesis of (-)-chorismic acid (22%) from (-)-III and of (-)-shikimic acid (94%) from (-)-II is reported.
IT **76947-23-4DP**, esters **76985-85-8DP**, esters
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of, enantioselective, with cholesterol esterase and lipase)
IT **106861-59-0P 106861-60-3P**
RL: PREP (Preparation)
(prepn. of, by enzymic resoln. of racemates, for chorismic acid prepn.)
IT **76985-84-7P 106861-61-4P**
RL: PREP (Preparation)
(prepn. of, by enzymic resoln. of racemates, for shikimic acid prepn)
IT **76947-23-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(resoln. of, enzymic, in chorismic acid prepn.)
IT **76985-85-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(resoln. of, enzymic, in shikimic acid prepn.)

L12 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:184893 HCAPLUS
DOCUMENT NUMBER: 102:184893
TITLE: An improved synthesis of (.+-.)-methyl shikimate through stereoselective cis-dihydroxylation of (.+-.)-methyl 5.beta.-hydroxycyclohexa-1,3-dienoate under Prevost's reaction conditions
AUTHOR(S): Campbell, Malcolm M.; Sainsbury, Malcolm; Yavarzadeh, Roya
CORPORATE SOURCE: Sch. Chem., Univ. Bath, Bath, BA2 7AY, UK
SOURCE: Tetrahedron (1984), 40(24), 5063-70
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:184893
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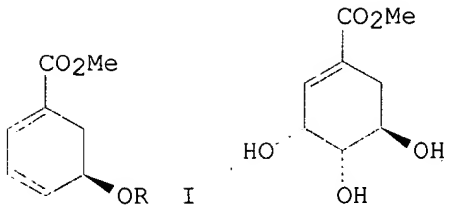

I II

AB A Prevost-type reaction under "wet" conditions upon the (.+-.)-Me 5.beta.-hydroxycyclohexa-1,3-dienoate deriv. I (R = Me3CSiMe2) gives (.+-.)-Me 3.alpha.-acetoxy-4.beta.-hydroxy-5.beta.-(tert-butyldimethylsilyloxy)cyclohexene which may be readily deprotected to afford (.+-.)-Me shikimate (II) in very high yield. Less selectivity is obsd. in a similar reaction upon I (R = H) and when this compd. is reacted under dry conditions the major product is (.+-.)-Me 4.beta.,5.beta.-epoxy-3.beta.-acetoxycyclohexenoate. An anal. of Prevost reactions with exo- and endo-Me 7-oxabicyclo[2.2.1]hept-5-en-2-oate is also described.

IT **76985-85-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L12 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:539381 HCAPLUS
DOCUMENT NUMBER: 99:139381
TITLE: Improved synthesis of racemic chorismic acid. Claisen rearrangement of 4-epi-chorismic acid and dimethyl 4-epi-chorismate
AUTHOR(S): Hoare, John H.; Policastro, Peter P.; Berchtold, Glenn A.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of the American Chemical Society (1983), 105(20), 6264-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
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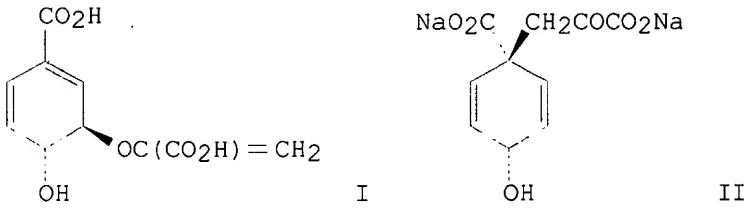

I II

AB The total synthesis of racemic chorismic acid (I) in 11 steps (6% overall yield) from Me 3-cyclohexenecarboxylate is described. Di-Me 4-epi-chorismate and 4-epi-chorismic acid were prepd. by similar procedures and their rates of Claisen rearrangement were studied. A convenient prepn. of di-Na prephenate (II) and di-Na 4-epi-prephenate from di-Me chorismate and 4-epi-chlorismate resp., is described.

IT **76947-23-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation with diazomalonate)

IT **76985-85-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and condensation with oxomalonate)

L12 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:406579 HCAPLUS
DOCUMENT NUMBER: 95:6579
TITLE: (-)-Methyl cis-3-hydroxy-4,5-oxycyclohex-1-enecarboxylate: stereospecific formation from and conversion to (-)-methyl shikimate; complex formation with bis(carbomethoxy)hydrazine
AUTHOR(S): McGowan, Donald A.; Berchtold, Glenn A.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Organic Chemistry (1981), 46(11), 2381-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB (-)-Me shikimate (I) reacts with Ph3P-EtO2CN:NCO2Et to afford the title compd. [(-)-II]. When the reaction is run with MeO2CN:NCO2Me, (-)-II is obtained as a 2:1 complex with MeO2CNHNHCO2Me. Solvolysis of (-)-II in aq. HOAc and cleavage of the acetate with MeO--MeOH affords (-)-I in high yield.
IT **76985-84-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and solvolysis of)
IT **76947-23-4P 76985-85-8P 77026-72-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

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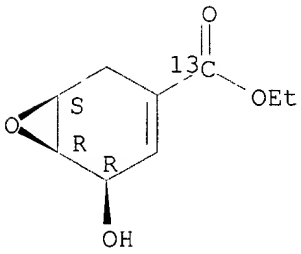
L11 ANSWER 1 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 241465-24-7 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic-13C acid, 5-hydroxy-, ethyl ester, (1S,5R,6R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C9 H12 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

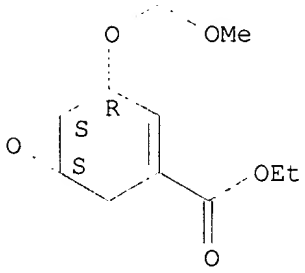


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:199546

L11 ANSWER 2 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 227599-99-7 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-(methoxymethoxy)-, ethyl ester, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H16 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Relative stereochemistry.



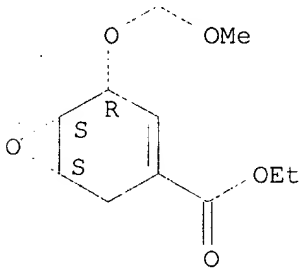
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:44605

L11 ANSWER 3 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221386-93-2 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-(methoxymethoxy)-, ethyl ester, (1S,5R,6S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H16 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

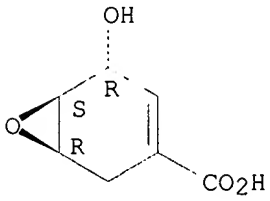
REFERENCE 1: 131:228949

REFERENCE 2: 130:237807

L11 ANSWER 4 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 213027-96-4 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, (1R,5R,6S)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C7 H8 O4
SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:232486

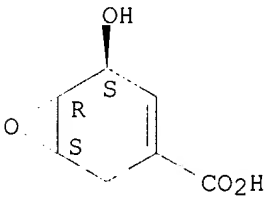
REFERENCE 2: 132:151600

REFERENCE 3: 132:22896

REFERENCE 4: 129:244668

L11 ANSWER 5 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 206537-16-8 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, (1S,5S,6R)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, [1S-(1.alpha.,5.alpha.,6.alpha.)]-
FS STEREOSEARCH
MF C7 H8 O4
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

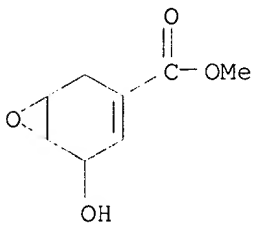
REFERENCE 1: 137:232486

REFERENCE 2: 132:151600

REFERENCE 3: 129:244668

REFERENCE 4: 128:319046

L11 ANSWER 6 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 200182-30-5 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H10 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

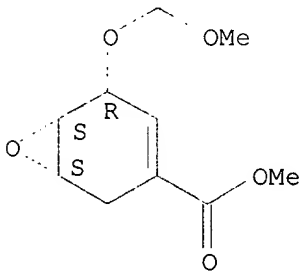
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:177332

REFERENCE 2: 128:61662

L11 ANSWER 7 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 187226-87-5 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-(methoxymethoxy)-, methyl ester, (1S,5R,6S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-(methoxymethoxy)-, methyl ester, [1S-(1.alpha.,5.beta.,6.alpha.)]-
FS STEREOSEARCH
MF C10 H14 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:337724

REFERENCE 2: 131:228949

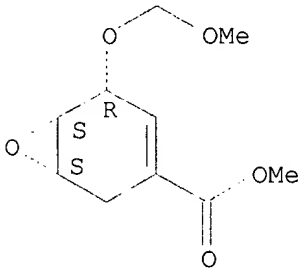
REFERENCE 3: 130:237807

REFERENCE 4: 129:54135

REFERENCE 5: 126:171813

L11 ANSWER 8 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 182368-11-2 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-(methoxymethoxy)-, methyl ester, (1.alpha.,5.beta.,6.alpha.)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H14 O5
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Relative stereochemistry.



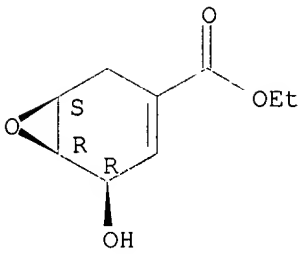
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:300503

L11 ANSWER 9 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 182367-90-4 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, ethyl ester, (1R,5S,6S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, ethyl ester, (1.alpha.,5.beta.,6.alpha.)-
FS STEREOSEARCH
MF C9 H12 O4
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

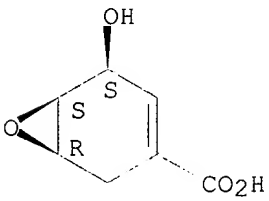
REFERENCE 1: 136:279213

REFERENCE 2: 131:44605

REFERENCE 3: 125:300503

L11 ANSWER 10 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 171596-14-8 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, (1R,5S,6S)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, [1R-(1.alpha.,5.beta.,6.alpha.)]-
OTHER NAMES:
CN Doederleinic acid
FS STEREOSEARCH
MF C7 H8 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

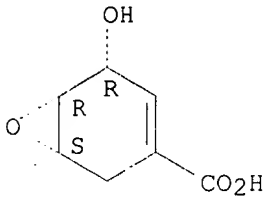
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 124:25613

L11 ANSWER 11 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 149560-23-6 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, [1S-(1.alpha.,5.beta.,6.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C7 H8 O4

SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

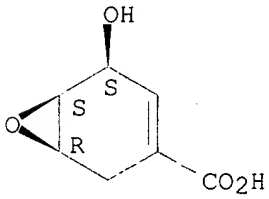
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:331672

REFERENCE 2: 119:139650

L11 ANSWER 12 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 127943-88-8 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-,
(1.alpha.,5.beta.,6.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-,
(1.alpha.,5.beta.,6.alpha.)-(.+-.)-
FS STEREOSEARCH
MF C7 H8 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

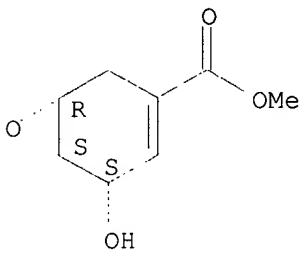
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 113:54938

L11 ANSWER 13 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 106861-61-4 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester,
(1R,5S,6S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester,

[1R-(1.alpha.,5.beta.,6.alpha.)]-
FS STEREOSEARCH
MF C8 H10 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:177332

REFERENCE 2: 114:159625

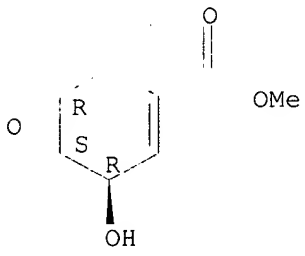
REFERENCE 3: 113:54938

REFERENCE 4: 110:188330

REFERENCE 5: 106:172361

L11 ANSWER 14 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 106861-60-3 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1R,5R,6S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, [1R-(1.alpha.,5.alpha.,6.alpha.)]-
FS STEREOSEARCH
MF C8 H10 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:232486

REFERENCE 2: 133:177332

REFERENCE 3: 132:151600

REFERENCE 4: 132:22896

REFERENCE 5: 129:244668

REFERENCE 6: 125:143175

REFERENCE 7: 116:41162

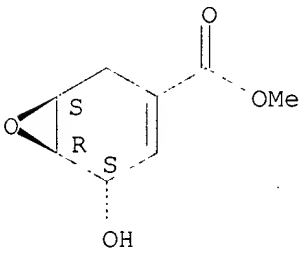
REFERENCE 8: 114:23661

REFERENCE 9: 113:23496

REFERENCE 10: 107:73150

L11 ANSWER 15 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 106861-59-0 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1S,5S,6R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, [1S-(1.alpha.,5.alpha.,6.alpha.)]-
FS STEREOSEARCH
MF C8 H10 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:232486

REFERENCE 2: 133:43373

REFERENCE 3: 132:22896

REFERENCE 4: 114:159625

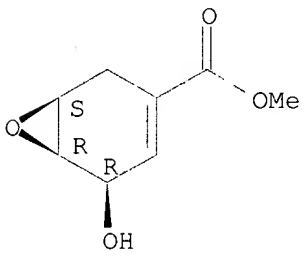
REFERENCE 5: 106:172361

L11 ANSWER 16 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 77026-72-3 REGISTRY
CN 1,2-Hydrazinedicarboxylic acid, dimethyl ester, compd. with [1S-(1.alpha.,5.beta.,6.alpha.)]-methyl 5-hydroxy-7-oxabicyclo[4.1.0]hept-3-ene-3-carboxylate (1:2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, [1S-(1.alpha.,5.beta.,6.alpha.)]-, compd. with dimethyl 1,2-hydrazinedicarboxylate (2:1) (9CI)
FS STEREOSEARCH
MF C8 H10 O4 . 1/2 C4 H8 N2 O4
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

CM 1

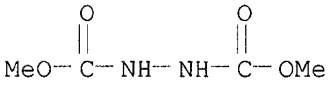
CRN 76985-84-7
CMF C8 H10 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 17643-54-8
CMF C4 H8 N2 O4



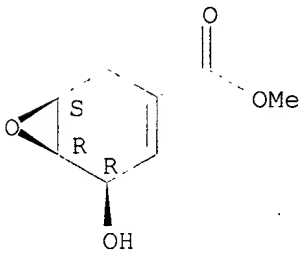
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 95:6579

L11 ANSWER 17 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 76985-85-8 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1R,5S,6S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1.alpha.,5.beta.,6.alpha.)-(.+-.)-
OTHER NAMES:

CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1.alpha.,5.beta.,6.alpha.)-
FS STEREOSEARCH
MF C8 H10 O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:153408

REFERENCE 2: 125:300503

REFERENCE 3: 110:188330

REFERENCE 4: 106:172361

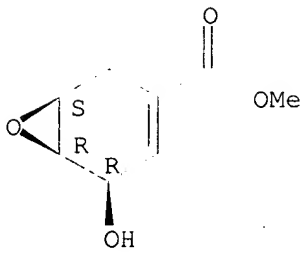
REFERENCE 5: 102:184893

REFERENCE 6: 99:139381

REFERENCE 7: 95:6579

L11 ANSWER 18 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 76985-84-7 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1S,5R,6R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, [1S-(1.alpha.,5.beta.,6.alpha.)]-
FS STEREOSEARCH
MF C8 H10 O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

16 REFERENCES IN FILE CA (1907 TO DATE)
16 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:337724

REFERENCE 2: 133:43373

REFERENCE 3: 132:151600

REFERENCE 4: 132:22896

REFERENCE 5: 131:228949

REFERENCE 6: 130:237807

REFERENCE 7: 129:244668

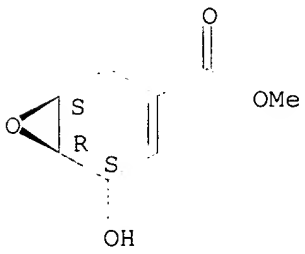
REFERENCE 8: 129:54135

REFERENCE 9: 128:319046

REFERENCE 10: 126:171813

L11 ANSWER 19 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 76947-23-4 REGISTRY
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1.alpha.,5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-Oxabicyclo[4.1.0]hept-3-ene-3-carboxylic acid, 5-hydroxy-, methyl ester, (1.alpha.,5.alpha.,6.alpha.)-(.+-.)-
FS STEREOSEARCH
MF C8 H10 O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 113:54938

REFERENCE 2: 110:23609

REFERENCE 3: 106:172361

REFERENCE 4: 99:139381

REFERENCE 5: 95:6579